Nuclear cell biology

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How does the nucleus move within the cell? How is the nucleus compartmentalized? How is nuclear size maintained? How is chromatin organized within the nucleus? These are a few of the questions related to nuclear cell biology addressed by our Minisymposium.

Dan Starr led off with a description of how nuclei migrate in *Caenorhabditis elegans*. A KASH protein in the outer nuclear membrane recruits microtubule motors to the nucleus. Live imaging of nuclear migration and microtubules suggests that kinesin-1 provides the major force to move nuclei. To resolve large cellular roadblocks, dynein mediates backward movements or dramatic nuclear rolling events (Fridolfsson and Starr, 2010).

G. W. Gant Luxton discussed mechanisms of nuclear migration in wounded cultured fibroblasts. Nesprin2G, SUN2, lamin, and actin cables associate in transmembrane actin-associated nuclear (TAN) lines to move nuclei (Luxton *et al.*, 2010). The AAA+ ATPase TorsinA disease gene regulates the formation of TAN lines and nuclear migration. TorsinA knockdown reduced the localization and mobility of Nesprin2G and disrupted nuclear migration, suggesting that TorsinA regulates SUN-KASH interactions in the nuclear envelope.

Levels of lamin-A/-C are known to increase during differentiation of embryonic stem cells (Constantinescu *et al.*, 2006). **Joe Swift** described new mass spectrometry methods to accurately measure the ratios of lamin-A/-C to lamin-B isoforms, which had not been directly measured previously. The findings are just beginning to enhance our understanding of lamin changes throughout development and aging.

Dan Levy described using *Xenopus laevis* and *tropicalis* as model organisms with similar DNA content but differently sized nuclei to understand nuclear scaling. Sperm nuclear assembly in *tropicalis* and *laevis* egg extracts mixed to different proportions directly correlated with nuclear size, suggesting size control by an egg cytoplasmic factor (Levy and Heald, 2010). Amounts of importin-α, Ntf2, and lamin were all involved in nuclear scaling. Future analyses will identify additional nuclear size factors and show how changes in size affect genome function.

Jason Brickner described mechanisms of targeting a gene to the nuclear periphery in yeast. Genes were localized by LacO repeats and GFP-LacI. Mutational analyses revealed DNA elements that function as "DNA zip codes" to promote targeting to the nuclear periphery through association with the nuclear pore complex (Ahmed *et al.*, 2010). A different DNA zip code controls posttranscriptional intranuclear targeting of the INO1 gene. This "memory" zip code is necessary and sufficient for H2A.Z incorporation and priming for reactivation (Light *et al.*, 2010). Specific zip codes may also promote long-range interchromatin interactions between genomic regions sharing the same elements.

Finally, **Ana Pombo** described how changes in chromatin positioning accompany gene activation, using the human uPA gene (Ferrai *et al.*, 2010). Prior to induction, uPA alleles are found at the interior of their chromosome territory, associated with poised transcription factories characterized by RNA polymerase II phosphorylation on Serine5, but not Serine2. Gene activation with phorbol esters induced uPA gene repositioning out of its chromosome territory. Investigation of a looping requirement for transcriptional activation showed that gene looping is not required for activity upon induction, but that the internal chromosome territory position prior to activation is important for reinforcing the silent state.

The Minisymposium on Nuclear Cell Biology covered the breadth of nuclear research, from events that control nuclear positioning within cells, to nuclear size control, to chromatin positioning and gene regulation. Future studies will focus on how nuclear position and size influence genome function, how nuclear envelope components might regulate the peripheral localization of individual loci, and how gene activity is regulated in different areas of the nucleus. We therefore look forward to future ASCB programs highlighting nuclear cell biology.

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DOI: 10.1091/mbc.E10-12-0966
Molecular Biology of the Cell Volume 22 Page 722
MBoC is pleased to publish this summary of the Minisymposium "Nuclear Cell Biology" held at the American Society for Cell Biology 2010 Annual Meeting, Philadelphia, PA, December 14, 2010.

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